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10/516,330	09/22/2005	Pascale Gaillard	262905US0PCT	8644

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EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	PAPER NUMBER
1624	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/516,330	GAILLARD ET AL.	
	Examiner	Art Unit	
	/Venkataraman Balasubramanian/	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20 and 22-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20 and 22-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/18/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I, claims 1-20 and 22-26, drawn to a compound of formula 1, wherein X=S and A is pyrimidinyl group, composition and method of use in the reply filed on 10/26/2007 is acknowledged. Claims 1-20 and 22-26 will be examined to the extent they embrace the elected subject matter. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

References cited in the Information Disclosure Statement, filed on 2/18/2005, are made of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20 and 22-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Recitation of "derivative" in claims 1-20 and 22-26 renders these claims indefinite as the term derivative implies more than what is being positively recited therein. Note a derivative can be any organic core or group bearing the azole core, thus the structural make-up of the genus remains unknown. An azole compound is suggested.

2. Recitation of sulfonyl, sulfonyl and sulfonamide" in claims 1 and 8 renders these claims and the dependent claims 2-7, 9-11,13-20 and 22-26 indefinite as these are divalent groups and what else is appended to these groups to meet the valence requirement is unclear.

3. Claims 23, 24 and 25 are indefinite as the variable groups are not defined properly. In claim 23, label X is not defined and whereas in claim 1, the nitrogen is substituted , in claim 23 it is not. In claim 24, X and A' are not defined. It refers to A which is not in the compounds shown therein. In claim 25, various variable groups are not defined. It refers to A and Y which are not present in the formula shown therein.

4. Recitation of "at least on disease" and " an amount sufficient to treat at least one disease" in claim 14 and " at least one disease" in claims 15-16, renders these claims indefinite as it is not clear what is intended. As recited, it implies that the method is meant for treating more than one disease at a given time with effective amount sufficient to treat one disease.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for diabetes and obesity does not reasonably provide enablement for treating various diseases embraced in claim 14 and any or all diseases mediated by any or all kinases generically embraced in claim 18. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Following apply.

The instant method of use claim 18 is drawn to "a method of treating a disease mediated by protein kinase activity and thereby treating any or all diseases including cancer, bacterial and viral infections, inflammatory and autoimmune diseases, cardiovascular diseases, nephrological diseases and chronic and acute neurodegenerative diseases. Claim 14 includes various diseases which again appear to be based on the mode of action of the instant compounds as protein kinase inhibitors. These diseases include at least one disease selected from the group consisting of neurodegenerative diseases, neuronal disorders including epilepsy, Alzheimer's disease, Parkinson's disease, retinal diseases, spinal cord injury, head trauma, mood disorders, particularly bipolar mood disorder, multiple sclerosis or amyotrophic lateral sclerosis, diabetes, particularly type II diabetes and obesity, asthma, septic shock, transplant rejection, cerebrovascular accident, glaucoma, cardiovascular diseases including stroke, arteriosclerosis, myocardial infarction, myocardial reperfusion injury, ischemic disorders, cancer and inflammatory diseases including arteriosclerosis, arthritis, Inflammatory Bowel Disease and rheumatoid arthritis,

Instant claims 14 and 18 , as recited, are a reach through claim. A reach through claim is a claim drawn to a mechanistic, receptor binding or enzymatic functionality in general format and thereby reach through a scope of invention for which they lack adequate written description and enabling disclosure in the specification.

In the instant case, based on the inhibition of protein kinase in general and c-Jun kinase and Glycogen Synthase Kinase (GSK-3) by the instant compounds, claims 14 and 18 reach through treating any or all diseases . Such disease would include cancers, bacterial and viral infections, inflammatory and autoimmune diseases, cardiovascular diseases, nephrological diseases and chronic and acute neurodegenerative diseases in general and thereby they lack adequate written description and enabling disclosure in the specification.

More specifically, in the instant case, based on the mode of action of instant compounds as inhibitor of protein kinase, based on limited assay with limited enzyme, it is claimed that treating and or preventing any or all cancer, infections, inflammatory and autoimmune diseases in general. The scope of the claims includes not only any or all disorders but also those condition yet to be discovered as mediated by any kinase. for which there is no enabling disclosure. In addition, the scope of these claims includes treatment of various diseases, which is not adequately enabled solely based on the inhibition of kinase provided in the specification .

In addition, the scope of claims includes treatment of various cancers which would include group consisting of lung cancer, bone cancer, pancreatic cancer, skin cancer. cancer of the head or neck, cutaneous or intraocular melanoma, uterine cancer,

ovarian cancer, rectal cancer, cancer of the anal region. stomach cancer, colon cancer, breast cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's disease, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, prostate cancer, chronic or acute leukemia, lymphocytic lymphomas, cancer of the bladder, cancer of the kidney or ureter, renal cell carcinoma, carcinoma of the renal pelvis, neoplasms of the central nervous system (CNS), primary CNS lymphoma, spinal axis tumors, brain stem glioma, pituitary adenoma, or a combination of one or more of the foregoing cancers, which is not adequately enabled solely based on the activity of the compounds provided in the specification.

Similarly, enablement for the scope of "inflammation" generally is not present. For a compound or genus to be effective against inflammation generally is contrary to medical science. Inflammation is a process, which can take place individually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There is no common mechanism by which all, or even most, inflammations arise. Mediators include bradykinin, serotonin, C3a, C5a, histamine, assorted leukotrienes and cytokines, and many, many others. Accordingly, treatments for inflammation are normally tailored to the particular type of inflammation present, as there is no, and there can be no "magic bullet" against inflammation generally. Inflammation is the reaction of vascularized

tissue to local injury; it is the name given to the stereotyped ways tissues respond to noxious stimuli. These occur in two fundamentally different types. Acute inflammation is the response to recent or continuing injury. The principal features are dilatation and leaking of vessels, and recruitment of circulating neurophils. Chronic inflammation or "late-phase inflammation" is a response to prolonged problems, orchestrated by T-helper lymphocytes. It may feature recruitment and activation of T- and B-lymphocytes, macrophages, eosinophils, and/or fibroblasts. The hallmark of chronic inflammation is infiltration of tissue with mononuclear inflammatory cells. Granulomas are seen in certain chronic inflammation situations. They are clusters of macrophages, which have stuck tightly together, typically to wall something off. Granulomas can form with foreign bodies such as aspirated food, toxocara, silicone injections, and splinters. Otitis media is an inflammation of the lining of the middle ear and is commonly caused by Streptococcus pneumoniae and Haemophilus influenzae. Cystitis is an inflammation of the bladder, usually caused by bacteria. Blepharitis is a chronic inflammation of the eyelids that is caused by a staphylococcus. Dacryocystitis is inflammation of the tear sac, and usually occurs after a long-term obstruction of the nasolacrimal duct and is caused by staphylococci or streptococci. Preseptal cellulitis is inflammation of the tissues around the eye, and Orbital cellulitis is an inflammatory process involving the layer of tissue that separates the eye itself from the eyelid. These life-threatening infections usually arise from staphylococcus. Hence, these types of inflammations are treated with antibiotics. Certain types of anti-inflammatory agents, such as non-steroidal anti-inflammatory medications (Ibuprofen and naproxen) along with muscle

relaxants can be used in the non-bacterial cases. The above list is by no means complete, but demonstrates the extraordinary breadth of causes, mechanisms and treatment (or lack thereof) for inflammation. It establishes that it is not reasonable to any agent to be able to treat inflammation generally.

The same applies to autoimmune diseases. The "autoimmune diseases" are a process that can take place in virtually any part of the body. There is a vast range of forms that it can take,' causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There are hundreds such diseases, which have fundamentally different mechanisms and different underlying causes. Thus, the scope of claims is extremely broad.

Again, it appears that, because the instant compounds inhibit kinase, it is recited implicitly that, based on the inhibition, any or all infections can be treated with the instant compounds for which there is no adequate written description and enabling disclosure. Infections in general can be by microorganisms and list of pathogenic microorganism is so large that a single class compound would not be effective for treating all infections. For example for bacteria, the list include gram-positive bacteria, including cocci such as Staphylococcus species and Staphylococcus species, acid-fast bacterium, including Mycobacterium species, bacilli, including Bacillus species, Corynebactedum species and Clostridium species, filamentous bacteria, including Actinomyces species and Streptomyces species', gram-negative bacteria, including cocci such as Neisseria species and Acinetobacter species, bacilli, such as Pseudomonas species, Brucella species, Agrobacterium species, Bordetella species,

Escherichia species, Shigella species, Yersinia species, Salmonella species, Klebsiella species, Enterobacter species, Haemophilus species, Pasteurella species, and Streptobacillus species, spirochetal species, Campy/obacter species, Vibrio species, and intracellular bacteria including Rickettsiae species and Chlamydia species. Specific bacterial species that are targets for the antibiotics of the invention include Staphylococcus aureus Staphylococcus epidermidis, Staphylococcus saprophyticus, Stœptococcus pyogenes; Streptococcus agalactiae, Stœptococcus pneumoniae, Enterococcus faecalis, Enterococcus faecium Bacillus anthracis, Mycobacterium avium, Mycobacterium tuberculosis, Acinetobacter baumannii; Corynebacterium diphtheria, Clostddium perfringens, Clostridium botulinum, Clostridium tetani, Neisseria gonorrhoeae, Neisseria meningitidis, Pseudomonas aeruginosa, Legionella pneumophila, Escherichia coli, Yersinia pestis, Haemophilus influenzae, Helicobacter pylori, Campylobacter fetus, Campylobacter jejuni, Vibrio cholerae, Vibrio parahemolyticus, Trepomena pallidum, Actinomyces israelli, Rickettsia prowazekii, Rickettsia rickettsii, Chlamydia trachomatis, Chlamydia psittaci, Brucella abortus, Agrobacterium tumefaciens; and Francisella tularensis, for which there is no adequate written description and enabling disclosure.

The same is true for viral infection. For example the list of various viral diseases due to DNA virus such as hepatitis B virus, herpes viruses (e.g., Herpes Simplex Virus, Cytomegalovirus (CMV), Epstein-Barr Virus, (EBV)), smallpox virus, or human papilloma virus (e.g., HPV), many human and animal pathogens: flaviviruses, such as dengue fever, West Nile, and yellow fever; pestiviruses, such as bovine viral diarrhea

(BVD), and hepaciviruses, such as hepatitis C; filoviruses such as ebola; parainfluenza viruses, including respiratory syncytial; rubulaviruses, such as mumps; morbillivirus, such as measles, picomaviruses, including the echoviruses; the coxsaclçieviruses; the polioviruses; the togaviruses, including encephalitis; coronaviruses, including Severe Acute Respiratory Syndrome (SARSI; rubella; bunyaviruses; reoviruses, including rotaviruses; rhabdoviruses; arenaviruses, such as lymphocytic choriomeningitis, as well as other RNA viruses of man and animal.

Applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended host. Moreover many if not most of diseases such as autoimmune diseases such as lupus, AIDS psoriasis, lung cancer, brain cancer, pancreatic cancer, colon cancer etc. are very difficult to treat and despite the fact that there are many agents whose mode of action is said to alleviate inflammation.

The scope of the claims involves millions of compounds of claim 1 as well as the thousands of diseases embraced by the terms cancer, bacterial and viral infection, autoimmune disease and inflammatory disease, cardiovascular diseases, nephrological diseases and chronic and acute neurodegenerative diseases.

Specific diseases group include: group consisting of inflammatory disease, rheumatoid arthritis, inflammatory bowel disease, asthma, dermatosis, psoriasis, atopic dermatitis, autoimmune diseases, tissue and organ rejection, Alzheimer's disease, stroke, epilepsy, Parkinson's disease, atherosclerosis, restenosis, cancer, Hodgkins disease, viral infection, AIDS infection, osteoarthritis, osteoporosis, and Ataxia

Telangiestasia. wherein said inflammatory or autoimmune condition is selected from the group consisting of rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gout, asthma, bronchitis, allergic rhinitis, chronic obstructive pulmonary disease, cystic fibrosis, inflammatory bowel disease, irritable bowel syndrome, mucous colitis, ulcerative colitis, diabrotic colitis, Crohn's disease, gastritis, esophagitis, hepatitis, pancreatitis, nephritis, psoriasis, eczema, dermatitis, hives, multiple sclerosis, Lou Gehrig's disease, sepsis, conjunctivitis, acute respiratory distress syndrome, purpura, nasal polip, lupus erythematosus, conjunctivitis, vernal catarrh, chronic arthrorheumatism, systemic inflammatory response syndrome (SIRS), sepsis, polymyositis, dermatomyositis (DM), Polyaritis nodoa (PN), mixed connective tissue disease (MCTD), and Sjoegren's syndrome, wherein said cardiovascular, metabolic, or ischemic condition is selected from the group consisting of atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, insulin resistance, Type I diabetes, Type II diabetes, hyperglycemia, hyperinsulinemia, dyslipidemia, obesity, polycystic ovarian disease, hypertension, syndrome X, osteoporosis, erectile dysfunction, cachexia, myocardial infraction, ischemic diseases of heart kidney, liver, and brain, organ transplant rejection, graft versus host disease, endotoxin shock, and multiple organ failure, wherein the viral infection is caused by a virus selected from the group consisting of human immunodeficiency virus (HIV), hepatitis B virus, hepatitis C virus, human papilomavirus, human T-cell leukemia virus, and Epstein-Barr virus.

As seen, instant compounds can be used for treating any disease which is a remarkable finding for which there is no adequate support in the specification.

No compound has ever been found to treat diseases of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "compound" is contrary to our present understanding of modern medicine. For example, as for cancer, Cecil Textbook of Medicine states, "each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004). Different types of cancers affect different organs and have different methods of growth and harm to the body. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally. Also see the PTO website

<<http ://www.uspto.gov/web/offices/pac/dapp/1 pecba.htm#7>>

ENABLEMENT DECISION TREE, Example F, situation 1) which is directed to the scope of cancers.

Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001 wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method treating solely based on the

inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. Mass, R. D., Int. J. Radiation Oncology Bio. Phys. Vol. 58(3): 932-940, 2004 and Fabbro et al. Pharmacology & therapeutics 93, 79-98, 2002. For fungal infection, see for example the two non-patent literature Turner et al., Current Pharmaceutical Design. 2, 209-224, 1996. and Sugar et al., Diagn. Microbiol. Infect. Dis. 21: 129-133, 1995. Both these references suggest the art is still exploratory and that a single agent may not be able function as antifungal agents for all fungal infection, despite the fact that large number of antifungal agents were known. For bacterial infection, see Snyder et al., J. Med. Liban 48(4): 208-214, 2000 (PubMed Abstract provided), wherein with regards to antibacterial therapies, it is stated that " common bacteria whose susceptibility to antimicrobials is no longer predictable". Note also that despite the fact there are several commercial antibacterial agents are available, it is still difficult to treat several pathogens such as those cause leprosy, meningitis, sexually transmitted infections, anthrax etc. The same is true for kinases in general. See Mass, R. D., Int. J. Radiation Oncology Bio. Phys.Vol. 58(3): 932-940, 2004, Fabbro et al. Pharmacology & therapeutics 93, 79-98, 2002. The state of the art is also indicative of the unpredictability of the therapeutic approach based on c-Jun kinase or GSK3 inhibiting activity. See Patel et al. Biochem. Soc. Trans. 32(5), 803-808,2004(PubMed Abstract provided), Jope et al., Trends in Biochemical Sciences, 20(2): 95-102, 2004 and Cohen et al., Nature Reviews/Molecular Biology 2: 769-776, 2001.

Also, note MPEP 2164.08(b) which states that claims that read on "... significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative.". Clearly that is the case here.

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating any or all diseases mediated by protein kinase including cancer, bacterial and viral infections, inflammatory and autoimmune diseases, cardiovascular diseases, nephrological diseases and chronic and acute neurodegenerative diseases as wellas various diseases recited in claim14 stated above that require kinase inhibitory activity.

2) The state of the prior art: Recent publications expressed that the kinase effects are unpredictable and are still exploratory. See Mass et al., and Fabbro, et al., cited above especially the concluding paragraph. See also Turner et al., Sugar et al., and Snyder et al., as well as Patel et al., Jope et al., and Cohen et al., cited above

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical

use for treating and or preventing any or all cancer, infections, inflammatory and autoimmune diseases, cardiovascular diseases, nephrological diseases and chronic and acute neurodegenerative diseases with the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show treating and or preventing any or all cancer, infections, inflammatory and autoimmune diseases, cardiovascular diseases, nephrological diseases and chronic and acute neurodegenerative diseases and the state of the art is that the effects of kinase inhibitors are unpredictable.

6) The breadth of the claims: The instant claims embrace any or all cancer, bacterial and viral infections, inflammatory and autoimmune diseases, cardiovascular diseases, nephrological diseases and chronic and acute neurodegenerative diseases related to kinase.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant

case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating and or preventing the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was 'filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-13, 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ambinter Exploratory Library 2002.

The IDS includes several catalog compounds which are excluded by proviso in claim 1.

While said compound(s) doesn't anticipate the scope of instant claims, they are very closely related as positional isomers of compounds of instant claims. However, positional isomers are not deemed patentably distinct absent evidence of superior or unexpected properties. See In re Crounse, 150 USPQ 554; In re Norris 84 USPQ 458; In re Finely 81 USPQ 383 and 387; Ex parte Engelhardt, 208 USPQ 343; Ex parte Henkel, 130 USPQ 474, regarding positional isomers.

Thus it would have been obvious to one skilled in the art at the time of the invention was made to expect instant compounds to possess the utility taught by the applied art in view of the close structural similarity outlined above.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

/Venkataraman Balasubramanian/

Primary Examiner, Art Unit 1624

1/5/2008